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09/576,715	05/23/00	HATAKEYAMA	K 2000 0644A

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EXAMINER	
FORMAN, B	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/576,715	Applicant(s) HATAKEYAMA, KAZUHISA	
	Examiner BJ Forman	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Action is in response to papers filed11 June 2001 in Paper No. 9 in which claims 1, 9-13 were amended. All of the amendments have been thoroughly reviewed and The previous rejections in the Office Action of Paper No. 7 dated 12 January 2001 35 U.S.C. 112, second paragraph in § b-e are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) are withdrawn in view of the amendments and new grounds for rejection. All of the arguments have been thoroughly reviewed but are mooted in view of the withdrawn rejections and new grounds for rejection.

Currently claims 1-13 are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-12 are indefinite in Claim 1 because the claims are drawn to a method for gene analysis but the claim does not recite method steps of gene analysis. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which others would be precluded. *Ex parte Erlich*, 3 USPQ2d 1011 at

6. It is suggested that Claim 1 be amended to recite positive active method steps for gene

analysis as described in the specification e.g. hybridizing, immobilizing, detecting, binding, quantifying, analyzing.

Claims 1-12 are indefinite in Claim 1 for the recitation "promoting hybridization having a function to stabilize" because it is unclear whether the "protein having a function to stabilize" also has a function of "promoting hybridization" or whether there is another protein which promotes the hybridization. The recitation is further indefinite because it is unclear the recitation is a method step of stabilizing or a characteristic of the protein. It is suggested that Claim 1 be amended to clarify e.g. replace "promoting hybridization" with "hybridizing" and replace "having a function to stabilize" with wherein said protein stabilizes".

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guagliardi et al. (M. Mol. Bio. 1997, 267: 841-848) in view of Dramanac (U.S. Patent No. 6,025,136, filed 28 August 1997) and SwisProt (accession No. 059631, 15 December 1998 and accession No. P39476; P81550, 1 February 1995).

Regarding Claim 1, Guagliardi et al. teach a method of gene analysis comprising: hybridizing a probe nucleic acid and sample nucleic acid in the presence of a double-stranded DNA binding protein wherein said protein stabilizes complementary double-stranded DNA and promotes hybridization (Abstract) and detecting the hybridization (page 842, Fig. 1) but they do

not teach immobilizing either the probe or the sample nucleic acid. However, probe immobilization in methods of gene analysis was well known in the art at the time the claimed invention was made as taught by Dramanac. Specifically, Dramanac teach a method of gene analysis comprising immobilizing the probe nucleic acid; adding the sample nucleic acid; promoting hybridization and detecting hybridization (Column 2, lines 44-52) and they teach the advantages of immobilizing the probes as claimed i.e. solves the problems of time required for identifying and sequencing by permitting simultaneous analysis of large sets of samples. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the solution hybridization of Guagliardi et al. with the array-immobilized probes for array-based hybridization and gene analysis for the expected benefits of economy of time and labor i.e. eliminates multiple hybridization assays by permitting analysis of thousands of samples simultaneously as taught by Dramanac (Column 2, lines 15-26). Additionally, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to detection of Dramanac wherein labeled probes are scored and normalized to accurately analyzed hybridization by adding the double-stranded DNA binding protein which promotes hybridization based on strict homology as taught by Guagliardi et al. to thereby reduce the time of hybridization and enhance specificity of hybridization by hybridizing at higher temperatures for the expected benefit of increasing speed and accuracy of gene analysis as taught by Guagliardi et al. (page 847, right column, lines 3-14).

Regarding Claim 2, Guagliardi et al. teach the method wherein the sample nucleic acid is DNA (page 843, Fig. 1) and Dramanac teaches the sample nucleic acid is DNA (Column 2, lines 15-27).

Regarding Claim 3, Guagliardi et al. teach the method wherein the a double-stranded DNA-binding protein is derived from a hyperthermophilic bacterium (page 843, right column, third full paragraph).

Regarding Claim 4, Guagliardi et al. teach the method wherein the a double-stranded DNA-binding protein is derived from an archaebacterium (page 841, right column, first full paragraph).

Regarding Claim 5, Guagliardi et al. teach the method wherein the a double-stranded DNA-binding protein is derived from a bacterium belonging to the genus *Sulfolubus* (page 841, right column, first full paragraph).

Regarding Claim 6, Guagliardi et al. teach the method wherein the a double-stranded DNA-binding protein is derived from *Sulfolubus solfataricus* (page 841, right column, first full paragraph).

Regarding Claim 7, Guagliardi et al. teach the method wherein the a double-stranded DNA-binding protein is the Sso7d protein derived from *Sulfolubus solfataricus* (page 841, right column, first full paragraph).

Regarding Claim 8, Guagliardi et al. teach the sequence of the Sso7d is known (page 841, right column, lines 9-18) and SwissProt specifically teaches the sequence accession No. 059631; P39476; and P81550) (Claim 8).

Regarding Claim 9, Guagliardi et al. teach the method wherein the sample nucleic acids are labeled (page 844, Fig. 2a, page 845, Fig. 3b and page 846, Fig 5).

Regarding Claim 10, Guagliardi et al. teach the method wherein the amount of target sequence is analyzed i.e. the intensity of the labeled nucleic acids bound and unbound to the DNA-binding proteins is analyzed to determine the amount of nucleic acids bound (% annealed product) (page 844, Fig. 2b and page 845, Fig. 3a & Fig. 4a).

Regarding Claim 11, Guagliardi et al. teach the method wherein the detection of hybridization is performed by using a plurality of probe nucleic acids and detecting the polymorphism in the target sequence by comparing the hybridization signal obtained from the hybridization (page 844, right column, first paragraph and page 845, Fig. 4) and wherein the

intensity of each hybridization signal is obtained and compared (page 845, Fig. 4, and page 842, Fig. 1).

Regarding Claim 12, Guagliardi et al. teach the method wherein the detection of hybridization is performed using a plurality of probes and detecting nucleotide sequence by comparing the hybridization signal (page 844, right column, first paragraph and page 845, Fig. 4) and wherein the intensity of each hybridization signal is obtained and compared (page 845, Fig. 4, and page 842, Fig. 1).

6. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guagliardi et al. (M. Mol. Bio. 1997, 267: 841-848) in view of Stratagene (catalog, 1988, page 39).

Regarding Claim 13, Guagliardi et al. teach the claimed reagents for detecting hybridization between a probe nucleic acid and a sample nucleic acid comprising: a target sequence complementary to the probe nucleic acid and a double-stranded DNA-binding protein which functions to stabilize complementary double-stranded DNA (page 482, Fig. 1) but they do not teach the reagents combined into a kit. Stratagene catalog teaches a motivation to combine reagents into kit format (page 39). It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Guagliardi et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. 2) The other service provided in a kit is quality control" (page 39, column 1).

Response to Arguments

7. Applicant's arguments regarding the previous rejection over Wagner et al. have been considered but are moot in view of the amendments, withdrawn rejections and new grounds for rejection.

The Declaration under 37 CFR 1.132 filed 12 June 2001 is insufficient to overcome the rejection of claims 1-13 because the showing is not commensurate in scope with the claims as set forth in the last Office action because it refer(s) only to the system described in the above referenced application and not to the individual claims of the application. The claims are drawn to a method of gene analysis comprising immobilizing either the probe or sample nucleic acid; hybridizing probe to sample nucleic acid; promoting hybridization; and detecting hybridization. While the Declaration illustrates comparing hybridization signals between perfect match and mismatch hybrids in the presence or absence of Sso7d, the Declaration does not illustrate the claimed method of gene analysis. Thus, there is no showing that the objective evidence of nonobviousness is commensurate in scope with the claims. See MPEP § 716.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this

application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
August 3, 2001

S. Zitomer